

USSN 07/800,364
Group Art Unit 1814
Filed: November 26, 1991

Page 36, line 11, delete "Figure 2" and insert --SEQ ID NO:13--, therefor.

Page 37, line 32, delete "#1 to #846 of Figure 2" and insert -- #8 to #853 of SEQ ID NO:13--, therefor.

In the Claims:

1. (once amended) An isolated DNA sequence [encoding a BMP-8 protein said DNA sequence] comprising [at least one of] the following sequences

a)

GTG CAC CTG CTG AAG CCG CAC GCG GTC CCG AAG GCG TGC TGC GCG CCC ACC
AAG CTG AGC GCC ACT TCC GTG CTC TAC TAC GAC AGC AGC AAC AAC GTC ATC
CTG CGC AAG CAC CGC AAC ATG GTG CTC CGC GCC TGC GGC TGC CAC (SEQ ID
NO: 7);

b)

GAC TGG GTC ATC GCC CCC CAA GGC TAC TCA GCC TAT TAC TGT GAA GGG GAG
TGC TCC TTC CCG CTG GAC TCC TGC ATG AAC GCC ACC AAC CAC GCC ATC CTG
CAG TCC CTG (SEQ ID NO: 9); and

c)

GAC GTC CAC GGC TCC CAC GGC CGG CAG GTG
TGC CGTCGG CAC GAG CTG AGC TTC CAG GAC CTG GGC TGG CTG (SEQ ID NO:
11).

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(d) the nucleotide sequence comprising nucleotide #1 through #843 of Figure 2 (SEQ ID NO:13); and

e) the nucleotide sequence comprising nucleotide #430 through #843 of Figure 2 (SEQ ID NO:13).

7. (twice amended) An isolated DNA sequence comprising the nucleotide sequence set forth in [Figure 2 (SEQ ID NO:13)] from nucleotide #[1]8 to #[843]850.

8. (twice amended) An isolated DNA sequence comprising the nucleotide sequence set forth in [Figure 2 (SEQ ID NO: 13)] from nucleotide #[430]434 through #[843]850.

9. (once amended) An isolated DNA comprising [T]the DNA sequence of ATCC #75010 [encoding BMP-8].

17. (once amended) A method [for producing a BMP-8 protein said method] comprising the steps of:

- (a) culturing a cell transformed with a vector comprising [having] a DNA sequence of claim 6 said DNA sequence in operative association with an expression control sequence therefor; and
- (b) recovering, isolating and purifying from said culture

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medium a protein encoded by said DNA sequence [characterized by the ability to induce cartilage and/or bone formation].

18. (once amended) A method [for producing a purified BMP-8 protein said method] comprising the steps of

- (a) culturing a cell transformed with a vector comprising [having] a DNA sequence of claim 9 in operative association with an expression control sequence therefor; and
- (b) recovering, isolating and purifying from said culture medium a protein encoded by said DNA sequence [characterized by the ability to induce cartilage and/or bone formation].

19. (twice amended) A method [for producing a purified BMP-8 protein said method] comprising the steps of:

- (a) culturing a cell transformed with a vector comprising [having] a DNA sequence comprising nucleotide #[1]8 through #[843]850 of [Figure 2] SEQ ID NO:13 said DNA sequence in operative association with an expression control sequence therefore; and
- (b) recovering, isolating, and purifying from said culture medium a protein characterized by an amino acid sequence comprising amino acid #[143]4 to #[281]142 of [Figure 2] (SEQ ID NO:14).

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Add new claims:

26. A method comprising the steps of:

- (a) culturing a cell transformed with a vector comprising a DNA sequence of claim 7 said DNA sequence in operative association with an expression control sequence therefor; and
- (b) recovering, isolating and purifying from said culture medium a protein encoded by said DNA sequence.

27. A method comprising the steps of:

- (a) culturing a cell transformed with a vector comprising a DNA sequence of claim 8 said DNA sequence in operative association with an expression control sequence therefor; and
- (b) recovering, isolating and purifying from said culture medium a protein encoded by said DNA sequence.

28. A DNA sequence encoding a protein comprising the following amino acid sequences:

- a) Arg-His-Glu-Leu-Tyr-Val-Ser-Phe-Gln-Asp-Leu-Gly-Trp-Leu-Asp-Trp-Val-Ile-Ala-Pro-Gln-Gly-Tyr (SEQ ID NO: 1);

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b) Leu-Ser-Ala-Thr-Ser-Val-Leu-Tyr-Tyr-Asp-Ser-Ser-Asn-
Asn-Val-Ile-Leu-Arg (SEQ ID NO: 2); and

c) Ala-Cys-Cys-Ala-Pro-Thr-Lys (SEQ ID NO: 3).

29. The DNA of claim 6 wherein said protein has a molecular weight of 28,000-38,000 daltons and under reducing conditions a molecular weight of 14,000-20,000 daltons.

30. The DNA of claim 28 wherein said protein has a molecular weight of 28,000-38,000 daltons and under reducing conditions a molecular weight of 14,000-20,000 daltons.

31. A vector comprising the DNA of claim 28.

32. A DNA sequence which hybridizes under stringent conditions to the sequence of claim 28 and encodes a BMP-8 protein.

33. A method comprising

a) culturing a cell transformed with a vector comprising a DNA of claim 28 in operative association with an expression control sequence therefor; and

b) recovering, isolating and purifying from said culture medium a BMP-8 characterized by the following sequences

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- i) Arg-His-Glu-Leu-Tyr-Val-Ser-Phe-Gln-Asp-Leu-Gly-Trp-
Leu-Asp-Trp-Val-Ile-Ala-Pro-Gln-Gly-Tyr (SEQ ID NO:
1);
- ii) Leu-Ser-Ala-Thr-Ser-Val-Leu-Tyr-Tyr-Asp-Ser-Ser-Asn-
Asn-Val-Ile-Leu-Arg (SEQ ID NO: 2); and
- iii) Ala-Cys-Cys-Ala-Pro-Thr-Lys (SEQ ID NO: 3);

34. A method for isolating a DNA sequence comprising

a) designing nucleotide probes based on the following amino
acid sequences

- 54
- i) Arg-His-Glu-Leu-Tyr-Val-Ser-Phe-Gln-Asp-Leu-Gly-Trp-
Leu-Asp-Trp-Val-Ile-Ala-Pro-Gln-Gly-Tyr (SEQ ID NO:
1);
- ii) Leu-Ser-Ala-Thr-Ser-Val-Leu-Tyr-Tyr-Asp-Ser-Ser-Asn-
Asn-Val-Ile-Leu-Arg (SEQ ID NO: 2);
- iii) Ala-Cys-Cys-Ala-Pro-Thr-Lys (SEQ ID NO: 3);

b) screening a selected library with said probes; and
isolating said DNA sequence from said library said DNA encoding a
protein comprising the sequences set forth in i) through iii).